0009586368 BIOSIS NO.: 199598054201
**Cytokines as potential vaccine adjuvants**
AUTHOR: Nohria Anju; Rubin Robert H (Reprint)
AUTHOR ADDRESS: Massachusetts Inst. Technol., Clin. Res. Cent., 40 Ames St., Build. E18-435, Cambridge, MA 02142-1308, USA**USA
JOURNAL: Biotherapy (Dordrecht) 7 (3-4): p261-269 1994 1994
ISSN: 0921-299X
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

**CpG-containing synthetic oligonucleotides promote B and** cytotoxic **T cell responses to protein antigen: A new class of vaccine adjuvants**
AUTHOR: Lipford Grayson B (Reprint); Bauer Marc; Blank Christian; Reiter Rudi; Wagner Hermann; Heeg Klaus
AUTHOR ADDRESS: Inst. Med. Microbiol., Immunol. Hygiene, Technical Univ. Munich, Trogerstr. 9, D-81675 Munich, Germany**Germany
JOURNAL: European Journal of Immunology 27 (9): p2340-2344 1997 1997
ISSN: 0014-2980
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

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**IL-12 is an effective adjuvant to recombinant vaccinia virus-based tumor vaccines. Enhancement by simultaneous B7-1 expression**
AUTHOR(S): Rao, Jay B.; Chamberlain, Ronald S.; Bronte, Vincenzo; Carroll, Miles W.; Irvine, Kari R.; Moss, Bernard; Rosenberg, Steven A.; Restifo, Nicholas P.
LOCATION: Howard Hughes Med. Inst.-Natl. Inst. Health Res. Scholars Program, Natl. Inst. Health, Bethesda, MD, 20892, USA
JOURNAL: J. Immunol. DATE: 1996 VOLUME: 156 NUMBER: 9 PAGES: 3357-65
CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English

**Nonviable bacterial antigens administered with IL-12 generate antigen-specific T cell responses and protective immunity against Listeria monocytogenes**
AUTHOR(S): Miller, Mark A.; Skeen, Marianne J.; Ziegler, H. Kirk
LOCATION: Dep. Microbiol. Immunol., Emory Univ. Sch. Med., Atlanta, GA, 30322, USA
JOURNAL: J. Immunol. DATE: 1995 VOLUME: 155 NUMBER: 10 PAGES: 4817-28
CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English

0010932184 BIOSIS NO.: 199799566244
**Interleukin-15 acts as an immunological co-adjuvant for liposomal antigen in vivo**
AUTHOR: Gursel Mayda (Reprint); Gregoriadis Gregory
AUTHOR ADDRESS: Centre Drug Delivery Res., Sch. Pharmacy, Univ. London, 29-39 Brunswick Square, London WC1N 1AX, UK**UK
JOURNAL: Immunology Letters 55 (3): p161-165 1997 1997
ISSN: 0165-2478
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

**itle: HUMORAL AND CELLULAR IMMUNE-RESPONSES IN THE MURINE RESPIRATORY-TRACT FOLLOWING ORAL IMMUNIZATION WITH CHOLERA-TOXIN OR**

**ESCHERICHIA-COLI HEAT-LABILE ENTEROTOXIN** (Abstract Available)
Author(s): RUEDL C; RIESER C; KOFLER N; WICK G; WOLF H
Corporate Source: INNSBRUCK UNIV,SCH MED,INST GEN & EXPTL PATHOL,FRITZ PREGL STR 3-4/A-6020 INNSBRUCK//AUSTRIA/
Journal: VACCINE, 1996, V14, N8 (JUN), P792-798
ISSN: 0264-410X
Language: ENGLISH Document Type: ARTICLE
Abstract: Cholera toxin (CT) and Escherichia coli heat-labile enterotoxin (LT) are the strongest mucosal immunogens identified to date and are also good adjuvants when given orally together in combination with unrelated antigens. We used these potent immunogens to monitor focal and systemic immune responses following oral immunization of BALB/c mice, and compared their action on the following: (a) immunoglobulin production rates (IgG, IgM and IgA) in mucosal inductive (Peyer's patches-PPs), effector (intestinal lamina propria-LP, respiratory tract) and systemic (spleen) sites; (b) analysis of systemic antigen-specific antibodies (IgG subclasses, IgA and IgE); (c) time monitoring of fecal anti-CT and anti-LT antibodies, and (d) in vivo relevance of interleukin-6 (IL-6) to mucosal responses. Both mucosal immunogens elicited specific antibody responses (IgA, IgG) not only in the gastrointestinal tract (PP's and intestinal LP), but also in the respiratory tract and spleens of orally immunized mice. These mucosal responses were accompained by elevated secretion of IL-6 in all investigated tissues, indicating involvement of this cytokine in B-cell maturation processes. Furthermore, oral immunization with CT and LT induced elevated serum titers of IgG1 followed by IgG2a, IgG2b, IgG3 and IgA, while high antigen-specific IgA and IgG1 responses were found in fecal extracts. These findings illustrate the action of orally administered CT and LT, respectively, on several humoral and cellular immune responses not only at the gastrointestinal tract, the application sire, but also in distant mucosal effector sites such as the respiratory tract. These data suggest the potential use of these mucosal adjuvants in oral immunization strategies to improve the local immune response in remote mucosal tissues, in accordance with the concept of a common mucosa-associated immune system. Copyright (C) 1996 Elsevier Science Ltd.

**Detection of precursor T(h) cells in mesenteric lymph nodes after oral immunization with protein antigen and cholera toxin**
Schaffeler M.P.; Brokenshire J.S.; Snider D.P.
D.P. Snider, Department of Pathology, Intestinal Disease Research Programm, HSC-3N26, McMaster University, 1200 Main Street West, Hamilton, Ont. L8N 3Z5 Canada
International Immunology ( INT. IMMUNOL. ) (United Kingdom) 1997, 9/10 (1555-1562)
CODEN: INIME ISSN: 0953-8178
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 47

**Title: New advances in microsphere-based single-dose vaccines** (ABSTRACT AVAILABLE)
Author(s): Hanes J (REPRINT) ; Cleland JL; Langer R
Corporate Source: JOHNS HOPKINS UNIV,SCH MED, DEPT ONCOL, 725 N WOLFE ST HUNTERIAN 817/BALTIMORE//MD/21205 (REPRINT); JOHNS HOPKINS UNIV,SCH MED, DEPT NEUROSURG/BALTIMORE//MD/21205; GENENTECH INC,PHARMACEUT R&D/S SAN FRANCISCO//CA/94080; MIT,DEPT CHEM ENGN/CAMBRIDGE//MA/02139
Journal: ADVANCED DRUG DELIVERY REVIEWS, 1997, V28, N1 (OCT 13), P97-119
ISSN: 0169-409X Publication date: 19971013

**The preferential induction of a Th1 immune response by DNA-based immunization is mediated by the immunostimulatory effect of plasmid DNA**

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JOURNAL: Cellular Immunology 179 (2): p97-106 1997 1997
ISSN: 0008-8749
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In the present study, we have investigated the T cell response to the **HBsAg** , normally secreted as multivalent **particles** , and to beta-galactosidase, a cytoplasmic antigen, delivered as plasmid DNAs. We found that **cytokines** characteristic of a Th1 phenotype are produced in mice immunized by these plasmid DNAs. Using repeated injections of low doses of purified antigen, we demonstrated that neither prolonged presence of the antigen nor site of immunization resulted in an immune response with characteristics resembling those obtained with DNA-mediated immunization. Analysis of immune responses induced in mice by coinjection of plasmid DNA and beta-galactosidase or **HBsAg** demonstrated that the coinjected DNA stimulated a Th1 response against the injected antigen. These data therefore strongly suggest that the strong immune response obtained after intramuscular DNA immunization was due to the adjuvant effect of the plasmid DNA which is also responsible for the selective activation of CD4+ T cells with a Th1 phenotype.

**Adjuvants that enhance priming of cytotoxic T cells to a Ksup b-restricted epitope processed from exogenous but not endogenous hepatitis B surface antigen**

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Journal: International Immunology, 11/7 (1093-1102), 1999, United Kingdom
CODEN: INIME
ISSN: 0953-8178
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NO. OF REFERENCES: 60

Intramuscular (i.m.) or s.c. injection of plasmid DNA encoding hepatitis a small surface antigen ( **HBsAg** ) primes potent MHC I-restricted cytotoxic T lymphocyte (CTL) responses in H-2(d) (BALB/c) and H-2sup b (C57BL/6) mice. In contrast, i.m. or s.c. injection of exogenous **HBsAg particles** without adjuvants primes CTL responses in 'high responder' H-2(d) but not 'low responder' H-2sup b mice. We have shown that processing of exogenous but not endogenous **HBsAg** generates the Ksup b-binding S208-215 peptide ILSPFLPL. This system allowed us to optimize conditions for stimulating murine CTL responses to exogenous antigen by identifying adjuvants that facilitate priming of Ksup b-restricted CTL by injecting recombinant **HBsAg particles** into 'low responder' H-2sup b mice. Synthetic oligodeoxynucleotides with immunostimulating sequences or the recombinant **cytokine** IL-12 efficiently enhanced priming of CTL to exogenous **HBsAg** . Hence, the adjuvanticity of DNA sequences that induce T(h)1 **cytokines** facilitate priming of MHC I-restricted T cell responses to exogenous antigen and are therefore of potential value in formulating vaccines designed to enhance CTL priming to exogenous antigen.

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Language: English Document Type: REVIEW
Abstract: Polymer microspheres have shown great

**Immunological adjuvants: Mechanisms of action and clinical applications**

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Expert Opinion on Investigational Drugs ( EXPERT OPIN. INVEST. DRUGS ) ( United Kingdom) 1996, 5/9 (1079-1099)
CODEN: EOIDE ISSN: 1354-3784
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

**Adjuvants** are a neglected aspect of **vaccine** formulations, prudent choice of which can enhance the immune response both quantitatively and qualitatively. This **review** details the evolution and current range of adjuvants, particularly those in clinical trials. The components of different adjuvants are outlined and the manner in which they are thought to work is discussed. Antigen processing is an essential requirement of any immune response and these mechanisms are discussed in the context of adjuvant action.

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